



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/664,225	09/18/2000	Mary Lynne Hedley	08191/013001	4277

7590 04/24/2002

Janis K Fraser PhD JD
Fish & Richardson P C
225 Franklin Street
Boston, MA 02110-2804

EXAMINER

NGUYEN, DAVE TRONG

ART UNIT	PAPER NUMBER
----------	--------------

1632

DATE MAILED: 04/24/2002

10

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.		Applicant(s)	
	09/664,225		HEDLEY ET AL.	
	Examiner		Art Unit	
	Dave Nguyen		1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 28 January 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-69 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-66, 68 and 69 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>4, 6, 8</u> . | 6) <input checked="" type="checkbox"/> Other: <i>detailed action</i> . |

Art Unit: 1633

Applicant's election without traverse of Group II (Claims 1-66, 68 and 69, drawn to a hybrid DNA encoding multiple epitope(s) of viral antigens, method of virally infected treatment by DNA applications) in the response filed on January 28, 2002 is acknowledged. In addition, the elected species designated as the combination of SEQ ID NO: 66, SEQ ID NO: 69, SEQ ID NO: 152, and SEQ ID NO: 154, the microspheres, and intramuscular administration, were provisionally elected by applicants in the response

Claims 1-7, 10-14, 53-67, drawn to a hybrid DNA encoding multiple epitope(s) of tumor antigens, method of cancer treatment by DNA applications, are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a diligently-filed petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(h).

Elected claims 1-7, 10-14, 53-66 are objected because the claims embrace non-elected invention. Cancellation of the non-elected subject matter from the elected claims is required.

Elected claims 1-66, 68 and 69, drawn to a hybrid DNA encoding multiple epitope(s) of viral antigens, method of virally infected treatment by DNA applications, are pending for examination.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Art Unit: 1633

Claims 60-66, are rejected under 35 U.S.C. 112, first paragraph, because the specification is enabling only for claims limited to:

1/ A nucleic acid encoding a hybrid polypeptide comprising a targeting signal sequence and three segments, wherein the three segments are either contiguous or are separated by a spacer amino acid or spacer peptide:

a/ the first segment having the amino acid sequence of a first portion of a naturally occurring protein of a pathogenic agent, the first segment being at least eleven amino acids in length and comprising two epitopes;

b/ the second segment having the amino acid sequence of a second portion of a naturally occurring protein of a pathogenic agent, the second segment being at least eleven amino acids in length and comprising two epitopes different from the epitopes of (a); and

c/ the third segment having the amino acid sequence of a third portion of a naturally occurring protein of a pathogenic agent, the third segment being at least eleven amino acids in length and comprising two epitopes different from the epitopes of (a) and (b);

provided that either

i/ the first, second and third portions are non-contiguous portions of the same naturally occurring protein, and the sum of the three portions constitutes less than 70% of the sequence of the naturally occurring protein; or

ii/ the first, second and third portions are portions of three different naturally occurring proteins of one or more pathogenic agents, protein

2/ A method of eliciting an immune response in a mammal, the method comprising administering intramuscularly to the mammal, or administering directly at a target tissue site containing antigen presenting cells of said mammal an effective amount of the nucleic acid of 1/.

3/ A method of eliciting an immune response in a mammal, the method comprising administering to the mammal an effective amount of microspheres comprising a polymeric matrix or shell and the nucleic acid of 1/.

Art Unit: 1633

The specification does not reasonably provide enablement for any other claimed embodiment, wherein any non-direct administration route is employed so as to target any tissue site containing any antigen presenting cell distant from the administration route. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

With respect to claims embracing any signal sequence, the as-filed specification only provides sufficient guidance for the making and use of a target signal sequence (page 28 of the specification) in the disclosed and claimed nucleic acids. Thus, it is not apparent how one skilled in the art makes and uses, without undue experimentation, any other signal sequence that is not described in the as-filed specification. With respect to methods of expressing MHC class I or MHC class II binding epitopes at any target site wherein any administration route is embraced, the specification does not provide sufficient guidance and/or evidences for one skilled in the art to reasonably extrapolate, without undue experimentation, from a simple murine model of transgenic HLA-A *0201/H2Kb mice showing CTL responses generated as a result of intramuscular injection of microspheres encapsulating DNA encoding a polyepitope HPV polypeptide to any other claimed embodiment as embraced by the breadth of claimed invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

The claimed invention which contemplates that any of the disclosed DNA constructs would exhibit a therapeutically immune effect in any mammal including a human (see claim 61) when administered using any route of administration in a subject. The state of the art exemplified by McCluskie *et al.* (Molecular Medicine, 5, pp. 287-300, 1999) indicates:

Art Unit: 1633

- "The route of deliver of the DNA vaccine can have an impact on the efficiency of transfection as well as the types and location of cells transfected, and thus potentially on the nature of the immune response" (page 295, column 1 bridging column 2);
- "More recent with antigen-encoding plasmids have shown that antigen expression does not continue indefinitely, but rather is lost by some immune-mediated mechanism around 2-3 weeks after DNA injection" (page 295, column 2, last paragraph); and
- A number of factors appear to influence the Th bias of the immune response, including (i) the antigen; (ii) the dose of antigen; (iii) whether the antigen is secreted, cytoplasmic, or membrane bound; (iv) the route and method of DNA administration; (v) the number of immunizations; (vi) the presence of CpG motifs; (vii) the haplotype of the mouse immunized; (viii) the presence of adjuvant; (ix) co-expression of cytokines; (x) whether DNA is formulated (e.g., with cationic liposomes); and (xi) rest period between immunizations (page 296, column 1).

Even if an animal model including a mouse model may show a desired immune response (CTL responses) by art-recognized intramuscular injection route, McCluskie *et al.* teach that "the realization that results in mice often do not predict the situation in humans has also led to a large number of DNA vaccine studies in non-human primates", that "IM injection of plasmid DNA vaccines, while highly immunogenic in mice...was found to be only relatively so in chimpanzees..., and especially not all in Aotus monkeys", and that "it is probably safe to say that any vaccine that works in a human will work in a mouse, but not necessarily vice versa" (page 296, column 2, second and third paragraphs). In addition and as to mucosal routes as embraced by the claims, McCluskie *et al.* teach that "the generally absent responses with the noninjected routes were not unexpected, as the mucosal surfaces are protective barriers, physiologically designed to limit uptake of bacteria, viruses, antigens" (page 296, column 1), and that "although non-human primate models are frequently used for development and testing of human vaccines, it is not clear how predictive they will be in the case of DNA vaccines where efficacy, by virtue of

Art Unit: 1633

the requirement first to transfect cells and express the antigen, relies on many factors other than immunological responses to the antigen" (page 297, column 1).

In view of the reasonable unpredictability of the state of the art of DNA immunization methods as indicated in the exemplified McCluskie *et al.* reference, one skilled in the art then turns this instant specification for guidance, however, other than simple CTL responses generated in transgenic mice which is not even a real world mammal intended for the contemplated utility, as the result an intramuscular injection of microspheres encapsulating plasmid vectors encoding HPV epitopes, the specification does not provide sufficient guidance and/or evidence to overcome the obstacles as disclosed in the state of the prior art.

Even if a partially protective and/or therapeutic response has been shown in mice using the exemplified protocol, it is not apparent as to how the murine model using one single species of HPV encoded plasmid encapsulated in microspheres is reasonably extrapolated to the full scope of the claimed invention including a human subject at risk or being infected by any pathogenic pathogen, particularly given that there is no evidence that the murine model is a general phenomenon for any other claimed embodiment, and given the doubts expressed in the art of record.

Furthermore and with respect to vaccination and/or therapy methods encompassing non-injection routes, *e.g.*, inhalation and oral administration, the state of the art exemplified by Cryz *et al.* (Vaccine, Vol. 14, 7, Vaccine Delivery Systems, Reports of the Expert Panels, pages 665-688) indicates that oral delivery of any vaccine to gastrointestinal cells, *e.g.*, M cells, so as to have a therapeutic effect, remains unpredictable at the time the invention was made (page 674, columns 1 and 2). More specifically, Cryz *et al.* teach:

"Effective delivery to the GALT [gastrointestinal associated lymphoid tissue] is predicated with enormous problems. While it is a relatively simple task to deliver particles to certain sites in the intestine, the efficiency of uptake is very low. Recent studies suggest that less than a fraction of one percent of particles are taken up and translocated. Indeed recent studies in the UK failed to demonstrate the presence of fluorescent particles in M-cells of human subjects after repeated dosing with particulate carriers. Attempts have been made to improve the efficiency of the

Art Unit: 1633

process by the use of particles carrying appropriate monoclonal antibodies or lectins but the results are not especially encouraging. The use of lipid vehicles could have some advantages. Not surprisingly, the gastrointestinal tract, because of its very nature, will be a less efficient site for particle uptake than other mucosal surfaces. The process of presentation of a particle to M-cells is obviously a statistical problem. How does a particle in the centre of the lumen, carrying a receptor for M-cell interaction, 'know' that there are M-cells in the vicinity?" (page 674, column 2).

Thus, it is not apparent how one skilled in the art, without undue experimentation, practices the full scope of the claimed invention, and/or uses the DNA immunization methods as claimed to provide an active immunity for any future protection and/or therapeutic efficacy against an infection by any and/or strains of a pathogenic organism, particularly on the basis of applicant's disclosure, and in view of the doubts expressed in the art of record at the time the invention was made.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-66, 68 and 69, rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are indefinite in the recitation of "signal sequence" because it is not apparent as to that exactly the "signal" is intended for the structural and/or function of the claimed nucleic acid sequences.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary

Art Unit: 1633

skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-66, 68 and 69, embracing the elected species designated as the combination of SEQ ID NO: 66, SEQ ID NO: 69, SEQ ID NO: 152, and SEQ ID NO: 154, microspheres containing a nucleic acid sequence encoding the combination of sequences of SEQ ID NO: 66, 69 152 and 154, and intramuscular administration of the nucleic acid sequences or the microspheres, are rejected under 35 USC 103(a) as being unpatentable over either Hedley *et al.* (US Pat No. 5,783,567) or US Patent No. 6,183,746 (where J. Collins constitutes as an another or distinct inventive entity), taken with either Boursnell *et al.* (US pat No. 5,719,054), or Boursnell *et al.* (US pat No. 5,719,054), Edwards *et al.* (US Pat No. 6,004,557), Dillner *et al.* (US Pat No. 5,932,412) and Bleul *et al.* (US Pat NO. 5,753,233).

Both Hedley *et al.* or Collins *et al.* teach a method of eliciting an immune response in a mammal, the method comprising administering to the mammal an effective amount of microspheres comprising a polymeric matrix or shell and a nucleic acid encoding a trafficking signal sequence and polyepitopes of HPV, wherein the nucleic acid encodes a hybrid polypeptide comprising a targeting signal sequence and polyepitopes of naturally occurring pathogenic proteins, wherein the epitopes are either contiguous or are separated by a spacer amino acid or spacer peptide:

and wherein the nucleic acid encodes at least a HPV epitope of at least 11 amino acids in length (Hedley *et al.*, e.g., columns 2, 6, 13, 14, 61-64) and Collins *et al.*, entire document).

Art Unit: 1633

Both Hedley *et al.* and Collins *et al.* do not teach the specific combination of HPV epitopes designated as SEQ ID NOS: 66, 69, 152 and 154 for use in the making the HPV polyepitope encoding plasmid containing microspheres.

However, at the time the invention was made, the concept of employing HPV polyepitope encoding vector is well recognized in the prior art as exemplified in Boursnell *et al.* (entire document, specially columns 2, 3, 5, and 8). In fact Boursnell *et al.* teach the HPV epitopes comprising SEQ ID NOS: 66, 69, 152, and 154 in SEQ ID NOS: 9 (comprising SEQ ID NO: 69), 10 (comprising both SEQ ID NOS 66 and 152) and 13 (comprising SEQ ID NO: 154). Furthermore, Edwards *et al.* (US Pat No. 6,004,557), Dillner *et al.* (US Pat No. 5,932,412) and Bleul *et al.* (US Pat NO. 5,753,233) are exemplified references that discloses the immunoreactive HPV epitopes of SeQ ID NOS 66, 69, 152, and 154, respectively in SEQ ID NO: 12 (Edwards *et al.*), SEQ ID NO: 157 (Dillner *et al.*), SEQ ID NO: 2 (Bleul *et al.*) and SEQ ID NO: 61 (Dillner *et al.*).

It would have been obvious for one of ordinary skill in the art at the time the invention was made to have employed any combination of HPV epitopes available in the prior art such as those disclosed in Boursnell *et al.* and or in Boursnell *et al.* taken with Edwards *et al.* (US Pat No. 6,004,557), Dillner *et al.* (US Pat No. 5,932,412) and Bleul *et al.* (US Pat NO. 5,753,233) in the DNA immunization methods of Hedley *et al.* or Collins *et al.* so as to increase an immune response against HPV in any target mammal. One of ordinary skill in the art would have been motivated to have employed the combination as recited in the elected species because the combination of the known epitopes are minor modifications and expected to provide an additive effect in increasing an immune response against HPV in a target mammal, as taught by Hedley *et al.*, Collins *et al.* and Boursnell *et al.*, and because Boursnell *et al.*, Edwards, Dillner *et al.* and Bleul *et al.* all teach that the epitopes comprising SEQ ID NOS 66, 69, 152 and 154 are immunoreactive to antibodies against HPV.

Thus, the claimed invention as a whole was *prima facie* obvious.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686

Art Unit: 1633

F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-66, 68 and 69, embracing the elected species designated as the combination of SEQ ID NO: 66, SEQ ID NO: 69, SEQ ID NO: 152, and SEQ ID NO: 154, microspheres containing a nucleic acid sequence encoding the combination of sequences of SEQ ID NO: 66, 69 152 and 154, and intramuscular administration of the nucleic acid sequences or the microspheres, are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1-81 of U.S. Patent No. 6,183,746, taken with either Boursnell *et al.* (US pat No. 5,719,054), and Hedley *et al.* (US Pat No. 5,783,567), or Boursnell *et al.* (US pat No. 5,719,054), Hedley *et al.* (US Pat No. 5,783,567), Edwards *et al.* (US Pat No. 6,004,557), Dillner *et al.* (US Pat No. 5,932,412) and Bleul *et al.* (US Pat NO. 5,753,233).

Although the conflicting claims are not identical, they are not patentably distinct from each other because .

US Patent No. 6,183,746 (where J. Collins constitutes as an another or distinct inventive entity), teach a method of eliciting an immune response in a mammal, the method comprising administering to the mammal an effective amount of microspheres comprising a polymeric matrix or shell and a nucleic acid encoding a trafficking signal sequence and an HPV epitope.

Collins *et al.* do not claim the specific combination of HPV epitopes designated as SEQ ID NOS: 66, 69, 152 and 154 for use in the making the HPV polyepitope encoding plasmid containing microspheres.

Art Unit: 1633

However, at the time the invention was made, the concept of employing HPV polyepitope encoding vector is well recognized in the prior art as exemplified in Boursnell *et al.* (entire document, specially columns 2, 3, 5, and 8). Plasmid vectors expressing polyepitope fragments of pathogenic proteins and complexes with microspheres are also taught in Hedley *et al.* In fact Boursnell *et al.* teach the HPV epitopes comprising SEQ ID NOS: 66, 69, 152, and 154 in SEQ ID NOS: 9 (comprising SEQ ID NO: 69), 10 (comprising both SEQ ID NOS 66 and 152) and 13 (comprising SEQ ID O: 154). Furthermore, Edwards *et al.* (US Pat No. 6,004,557), Dillner *et al.* (US Pat No. 5,932,412) and Bleul *et al.* (US Pat NO. 5,753,233) are exemplified references that discloses the immunoreactive HPV epitopes of SeQ ID NOS 66, 69, 152, and 154, respectively in SEQ ID NO: 12 (Edwards *et al.*), SEQ ID NO: 157 (Dillner *et al.*), SEQ ID NO: 2 (Bleul *et al.*) and SEQ ID NO: 61 (Dillner *et al.*).

It would have been obvious for one of ordinary skill in the art at the time the invention was made to have employed any combination of HPV epitopes available in the prior art such as those disclosed in Boursnell *et al.* and or in Boursnell *et al.* taken with Edwards *et al.* (US Pat No. 6,004,557), Dillner *et al.* (US Pat No. 5,932,412) and Bleul *et al.* (US Pat NO. 5,753,233) in the DNA immunization methods of as claimed in Collins *et al.* so as to increase an immune response against HPV in any target mammal. One of ordinary skill in the art would have been motivated to have employed the combination as recited in the elected species because the combination of the known epitopes are minor modifications and expected to provide an additive effect in increasing an combination of immune responses against HPV in a target mammal, as taught by Boursnell *et al.* and Hedley *et al.*, and because Boursnell *et al.*, Edwards, Dillner *et al.* and Bleul *et al.* all teach that the epitopes comprising SEQ ID NOS 66, 69, 152 and 154 are immunoreactive to antibodies against HPV.

Thus, the claimed invention as obvious variants of that of the Collins *et al.* patent.

No claim is allowed.

Art Unit: 1633

Any inquiry concerning this communication or earlier communications regarding the formalities should be directed to Patent Analyst Dianiece Jacobs, whose telephone number is **(703) 305-3388**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner *Dave Nguyen* whose telephone number is **(703) 305-2024**.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, *Deborah Reynolds*, may be reached at **(703) 305-4051**.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is **(703) 305-7401**.

Any inquiry of a general nature or relating to the status of this application should be directed to the *Group receptionist* whose telephone number is **(703) 308-0196**.

Dave Nguyen
Primary Examiner
Art Unit: 1632



**DAVE T. NGUYEN
PRIMARY EXAMINER**